

## CROSS-REFERENCE TO RELATED APPLICATIONS

This is a continuation of U.S. Patent Application Serial No. 09/180,783 filed on November 16, 1998, the content of which is relied upon and incorporated herein by reference in its entirety, and the benefit of priority under 37 U.S.C. § 120 is hereby claimed.

## IN THE SPECIFICATION:

Page 1, please replace the first paragraph at Line 5 with the following paragraph:

### BACKGROUND OF THE INVENTION:

#### (i) Field of the Invention

The present invention relates to a method for the diagnosis of diseases by genetic analysis, in particular the analysis of genes for subunits of the human guanine nucleotide-binding proteins (G proteins).

Page 1, please replace the second paragraph at Line 10 with the following paragraph:

#### (ii) Description of the Related Art

Heterotrimeric guanine nucleotide-binding proteins (G proteins) have an outstanding importance in intracellular signal transduction. They mediate the relaying of extracellular signals after stimulation of hormone receptors and other receptors which undergo a conformational change after receptor activation. This leads to activation of G proteins which may subsequently activate or inhibit intracellular effectors (e.g. ion channels, enzymes). Heterotrimeric G proteins consist of three subunits, the  $\alpha$ ,  $\beta$  and  $\gamma$  subunits. To date, several different  $\alpha$  subunits, 5  $\beta$  subunits and about 12  $\gamma$  subunits have been detected by biochemical and molecular biological methods

in re application of: SIFFERT,  
Application No.: Not yet assigned  
Filed: Herewith

Group:  
Examiner:

Not assigned  
Not yet assigned

(Continuation of 09/180,783 - Filed: 17 March 1999)

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cont

(Birnbaumer, L. and Birnbaumer, M. Signal transduction by G proteins: 1994 edition. *J. Recept. Res.* 15:213-252, 1995; Offermanns, S. and Schultz, G. Complex information processing by the transmembrane signaling system involving G proteins. *Naunyn Schmiedeberg's Arch. Pharmacol.* 350:329-338, 1994; Nürnberg, B., Gudermann, T., and Schultz, G. Receptors and G proteins as primary components of transmembrane signal transduction. Part 2. G proteins: structure and function. *J. Mol. Med.* 73:123-132, 1995; Neer, E.J. Heterotrimeric G proteins: Organizers of Transmembrane Signals. *Cell* 80:249-257, 1995; Rens-Domiano, S. and Hamm, H.E. Structural and functional relationships of heterotrimeric G-proteins. *FASEB J.* 9:1059-1066, 1995).

Page 1, please replace the fourth paragraph at Line 39 with the following paragraph:

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SUMMARY OF THE INVENTION:

We have found that a genetic modification in the gene for human G protein  $\beta 3$  subunits is suitable for the diagnosis of diseases. This genetic modification is particularly suitable for establishing the risk of developing a disorder associated with G protein dysregulation.

Page 2, please replace the second paragraph at Line 6 with the following paragraph:

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BRIEF DESCRIPTION OF THE DRAWING:

The figure depicts a comparison of genes from normotensives and hypertensives by restriction enzyme analysis.

Page 2, please insert the following as paragraph three (following the preceding paragraph):

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DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS:

The genetic modification which has been found is located in the gene for human G protein  $\beta 3$  subunit. This gene has been described by Levine et al. (Proc. Natl. Acad. Sci USA, 87, (1990)